Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 13 (in part), 14-15, 30-34, 36, 38, 39, 40 (in part), 41-46, 55 (in part), 56-57, 59, and 61-63, drawn to a method of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursors in a mammalian subject in vivo using a VEGF-C/D polypeptide.

Group II, claim(s) 16-19 and 21-24, drawn a method of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursors or oligodendrocyte precursor cells in vitro using a VEGF-C/D product (polypeptide).

Group III, claim(s) 25, drawn to purified and isolated neural cells or oligodendrocyte precursor cells.

Group IV, claim(s) 26-27 and 29, drawn a method of administering or transplanting neural cells/oligodendrocyte precursor cells treated with VEGF-C/D into a mammalian subject.

Group V, claim(s) 13 (in part), 40 (in part), 47, 50, 53-54, 55 (in part), 60, drawn to a method of promoting recruitment, proliferation, differentiation,

migration or survival of neural cells or neural precursors in a mammalian subject in vivo using a VEGF-C/D polynucleotide.

Group VI, claim(s) 64-65, 68, drawn to a composition comprising VEGF-C/D or VEGF-C/D in combination with PDGF-A/C.

Group VII, claim(s) 70-73, drawn to a method of inhibiting growth and progression of neuroblasmta and neural tumors in a subject by a composition comprising a VEGF-C/D inhibitor or a VEGF-C/D inhibitor in combination with PEGF-A/C inhibitor.

Group VIII, claim(s) 74 and 76-81, drawn to a method for screening for modulators of VEGF-C or VEGF-D stimulation of neural stem cells or neural precursor cells.

2. The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The 1st claimed invention is drawn to a method of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursors in a mammalian subject in vivo using a VEGF-C/D polypeptide, which is anticipated by WO01/76620 and WO03/024478 as found in International Search Report. WO01/76620 teaches a method of treating a dysfunction or neuronal cell death in the CNS in a subject by a composition comprising VEGF (VEGF-B, C, or D) wherein the CNS disorder includes neurodegenerative diseases, neural stem/progenitor cell, ischemic or

motor neuronal disorders such as Parkinson's, Alzheimer's, stroke, amyotrophic lateral sclerosis, spinal cord injury and uppor/lower motor neuron diseases. (see p. 6-10, in particular). WO03/024478 teaches a method of treating a patient suffering a CNS disorder by a composition comprising VEGF (VEGF-A, B, C, or D) and/or PDGF (PDGF-B, BB, AB, C, D, CC, DD, BC, AC, AD or BD) wherein the CNS disorder includes neurodegenerative diseases, neural stem/progenitor cell, ischemic or neuropsychiatric disorders such as Parkinson's, Alzheimer's, stroke, amyotrophic lateral sclerosis, spinal cord injury and schizophrenia etc. (see p. 5, in particular). Since the materials, steps and patients in the methods of WO01/76620 and WO03/024478 are identical to those in the instant claims, the effects recited in preamble are the inherent results of administration of VEGF-C/D to the patient. Therefore, claim 1 is anticipated by WO01/76620 and WO03/024478. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Thus, Applicant's inventions do not contribute a special technical feature when view over the prior art, they do not have a single inventive concept and so lack unity of invention.

In addition Group I is directed to a technical feature of a method of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursors in a mammalian subject in vivo using a VEGF-C/D polypeptide. Group II is directed to a technical feature of a method of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursors or oligodendrocyte precursor cells in vitro using a VEGF-C/D product (polypeptide). Group

III is directed to a technical feature of purified and isolated neural cells or oligodendrocyte precursor cells. Group IV is directed to a technical feature of a method of administering or transplanting neural cells/oligodendrocyte precursor cells treated with VEGF-C/D into a mammalian subject. Group V is directed to a technical feature of to a gene therapy of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursors in a mammalian subject using a VEGF-C/D polynucleotide. Group VI is directed to a technical feature of a composition comprising VEGF-C/D or VEGF-C/D in combination with PDGF-A/C. Group VII is directed to a technical feature of a method of inhibiting growth and progression of neuroblasmta and neural tumors in a subject by a composition comprising a VEGF-C/D inhibitor or a VEGF-C/D inhibitor in combination with PEGF-A/C inhibitor. Group VIII is directed to a technical feature of a method for screening for modulators of VEGF-C or VEGF-D stimulation of neural stem cells or neural precursor cells.

Therefore, the above Inventions do not share a common special technical feature as they comprise different steps and utilize different products, which demonstrates that each method has a different mode of operation and use of structurally and functionally divergent materials. Accordingly, Groups I-VIII are not so linked by the same or a corresponding special technical feature within meaning of PCT Rule 13.1 so as to form a single general inventive concept.

Species Election

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Neural stem cells or oligodendrocyte precursor cell:

C17.2 purified neural stem cells, HSN-1 cells, fetal pig cells, neural crest cells, bone marrow derived neural stem cells, hNT cells, a human neuronal progenitor cell line, oligodendrocyte CG-4 cells, SVG pl 2 fetal glial cell line, DBTRG-05MG glial cell line, purified oligodendrocyte precursor cells, isolated NG2 pr0teoglycan (NG2+ cells).

Diseases:

Alzheimer's disease, Parkinson's disease, Huntington's disease, motor neuron disease, Amyotrophic Lateral Sclerosis (ALS), dementia and cerebral palsy, demyelination in the nervous system, chronic inflammatory demyelinating polyradiculoneuropath7 (CIDP), neural trauma, neural injury, multiple sclerosis, phenylketonuria, periventricular leukomalacia (PVL) HIV-1 encephalitis (HIVE), Guillian Barre Syndrome (GBS), acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN),MADSAM (multifocal acquired demyelinating sensory and motor neuropathy, also know as Lewis-Sumner

syndrome),DADS (distal acquired demyelinating symmetric neuropathy), stroke-related injury, spinal cord injury, post-operative injury and brain ischemia.

Neurotherapeutic agents:

interferon gamma, nerve growth factor, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), neurogenin, brain derived neurotrophic factor (BDNF), thyroid hormone, bone morphogenic proteins (BMPs), leukemia inhibitory factor (LIF), sonic hedgehog, glial cell line-derived neurotrophic factor (GDNFs), vascular endothelial growth factor (VEGF), interleukins, interferons, stem cell factor (SCF), activins, inhibins, chemokines, retinoic acid and ciliary neurotrophic factor (CNTF), tacrine, donepezil, rivastigmine, galantamine, cholinesterase inhibitors/anti-cholinergics, anti- inflammatory drugs, dopamine agonists/levodopa (L-dopa), catechol-0-methyl-transterases (COMTs), amantadine, Selegiline, carbidopa, ropinirole, coenzyme Q10, Pramipexole.

VEGF-C/D inhibitors:

(a) a polypeptide comprising an extracellular fragment of VEGFR-2 that binds to VEGF- C/a polypeptide comprising an extracellular fragment of VEGFR-3 that binds to VEGF- C; (b) an antibody substance that immunoreacts with a VEGF-C polypeptide; (c) a VEGF-C antisense molecule/a VEGF-C siRNA.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims

subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. The claims are deemed to correspond to the species listed above in the following manner:

i. If any group from Groups II-IV is elected, Applicant is required under PCT Rule 13.2 to elect a single disclosed species of cells as set forth above recited in claims 17 and 18 for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

ii. If Group I or Group V is elected, Applicant is required under PCT Rule 13.2 to elect a single disclosed species of disease as set forth recited in claims 7-8, 33-34 for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 13 is generic.

iii. If Group I or Group V is elected, Applicant is required under PCT Rule 13.2 to elect a single disclosed species of neurotherapeutic agent as set forth above

recited in claims 59-62 for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

iii. If Group VII is elected, Applicant is required under PCT Rule 13.2 to elect a single disclosed species of VEGF-C/D inhibitor as set forth above recited in claims 71-72 for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 70 is generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The technical features of these species are different because they are different cells, different diseases and different molecules. For example, for molecules, each specific species differs with respect to its composition and structures. For cells, the cell contents and biological characteristics in different neural stem cells are different from those of oligodendrocyte precursor cells. Consequently the responses to different biomolecules are also different in these different types of cells. Therefore, these species do not share a common corresponding technical feature; and thus lack unity of invention.

In addition, for diseases, the etiology and potential molecular mechanisms underlying these disorders are different. For example, the pathology and etiologies of spinal cord injury are very different from those of Alzheimer's diseases as well as other recited diseases. The patient populations in each disease are also very different. For

example, the health status, the medication, the diagnosis, and the physiological condition in patients with spinal cord injury are very different from those with AD and other recited diseases. It requires different diagnoses, equipments, steps and treatments for these different groups of patients. Therefore, these different species of diseases do not share a common corresponding technical feature; and thus lack unity of invention.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
March 20, 2010

/Chang-Yu Wang/
Examiner, Art Unit 1649